

SEQUENCE LISTING



<110> Pecker, Iris
Vlodavsky, Israel
Feinstein, Elena

<120> POLYNUCLEOTIDE ENCODING A POLYPEPTIDE HAVING HEPARANASE ACTIVITY AND EXPRESSION
OF SAME IN GENETICALLY MODIFIED CELLS

<130> 01/22603

<150> US 08/922,170

<151> 1997-09-02

<150> US 09/109,386

<151> 1998-07-10

<150> PCT/US98/17954

<151> 1998-08-31

<160> 47

<170> PatentIn version 3.1

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35 40 45

Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
50 55 60

Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
65 70 75 80

Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
85 90 95

Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe
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Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys
 115 120 125

Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp
 130 135 140

Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys Phe
 145 150 155 160

Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
 165 170 175

Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
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Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
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Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser
 225 230 235 240

Gln Leu Gly Glu Asp Tyr Ile Gln Leu His Lys Leu Leu Arg Lys Ser
 245 250 255

Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg
 260 265 270

Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu
 275 280 285

Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr
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Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile
 305 310 315 320

Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly
 325 330 335

Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala
 340 345 350

Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys
 355 360 365

Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val
 370 375 380

Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro
 385 390 395 400

Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr
405 410 415

Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg
420 425 430

Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly
435 440 445

Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu
450 455 460

Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu
465 470 475 480

Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn
485 490 495

Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met
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Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser
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Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu
1 5 10 15
ctg ctc ctg ggg ccg ctg ggt ccc ctc tcc cct ggc gcc ctg ccc cga 155
Leu Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg
20 25 30
cct gcg caa gca cag gac gtc gtg gac ctg gac ttc ttc acc cag gag 203
Pro Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu
35 40 45
ccg ctg cac ctg gtg agc ccc tcg ttc ctg tcc gtc acc att gac gcc 251
Pro Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala
50 55 60
aac ctg gcc acg gac ccg cgg ttc ctc atc ctc ctg ggt tct cca aag 299
Asn Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys
65 70 75
ctt cgt acc ttg gcc aga ggc ttg tct cct gcg tac ctg agg ttt ggt 347
Leu Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly

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ttt gaa gag aga agt tac tgg caa tct caa gtc aac cag gat att tgc				443
Phe Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys	115	120	125	
aaa tat gga tcc atc cct cct gat gtg gag gag aag tta cgg ttg gaa				491
Lys Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu	130	135	140	
tgg ccc tac cag gag caa ttg cta ctc cga gaa cac tac cag aaa aag				539
Trp Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys	145	150	155	
ttc aag aac agc acc tac tca aga agc tct gta gat gtg cta tac act				587
Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr	160	165	170	175
ttt gca aac tgc tca gga ctg gac ttg atc ttt ggc cta aat gcg tta				635
Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu	180	185	190	
tta aga aca gca gat ttg cag tgg aac agt tct aat gct cag ttg ctc				683
Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu	195	200	205	
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Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly	210	215	220	
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Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly	225	230	235	
tcg cag tta gga gaa gat tat att caa ttg cat aaa ctt cta aga aag				827
Ser Gln Leu Gly Glu Asp Tyr Ile Gln Leu His Lys Leu Leu Arg Lys	240	245	250	255
tcc acc ttc aaa aat gca aaa ctc tat ggt cct gat gtt ggt cag cct				875
Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro	260	265	270	
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Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly	275	280	285	
gaa gtg att gat tca gtt aca tgg cat cac tac tat ttg aat gga cgg				971
Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg	290	295	300	
act gct acc agg gaa gat ttt cta aac cct gat gta ttg gac att ttt				1019
Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe	305	310	315	
att tca tct gtg caa aaa gtt ttc cag gtg gtt gag agc acc agg cct				1067
Ile Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro	320	325	330	335
ggc aag aag gtc tgg tta gga gaa aca agc tct gca tat gga ggc gga				1115
Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly	340	345	350	
gcg ccc ttg cta tcc gac acc ttt gca gct ggc ttt atg tgg ctg gat				1163
Ala Pro Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp	355	360	365	
aaa ttg ggc ctg tca gcc cga atg gga ata gaa gtg gtg atg agg caa				1211
Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln	370	375	380	

gta ttc ttt gga gca gga aac tac cat tta gtg gat gaa aac ttc gat 1259
Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp
385 390 395

cct tta cct gat tat tgg cta tct ctt ctg ttc aag aaa ttg gtg ggc 1307
Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly
400 405 410 415

acc aag gtg tta atg gca agc gtg caa ggt tca aag aga agg aag ctt 1355
Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu
420 425 430

cga gta tac ctt cat tgc aca aac act gac aat cca agg tat aaa gaa 1403
Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu
435 440 445

gga gat tta act ctg tat gcc ata aac ctc cat aac gtc acc aag tac 1451
Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr
450 455 460

ttg cgg tta ccc tat cct ttt tct aac aag caa gtg gat aaa tac ctt 1499
Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu
465 470 475

cta aga cct ttg gga cct cat gga tta ctt tcc aaa tct gtc caa ctc 1547
Leu Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu
480 485 490 495

aat ggt cta act cta aag atg gtg gat gat caa acc ttg cca cct tta 1595
Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu
500 505 510

atg gaa aaa cct ctc cgg cca gga agt tca ctg ggc ttg cca gct ttc 1643
Met Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe
515 520 525

tca tat agt ttt ttt gtg ata aga aat gcc aaa gtt gct gct tgc atc 1691
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gagttccaga gcttcgggag ggtgggggtac acttcagtat tacattcagt gtgggtgttct 780
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1899

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 35 40 45

Lys Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu
 50 55 60

Leu Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg
 65 70 75 80

Pro Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu
 85 90 95

Pro Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala
 100 105 110

Asn Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys
 115 120 125

Leu Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly
 130 135 140

Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr
 145 150 155 160

Phe Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys
 165 170 175

Lys Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu
 180 185 190

Trp Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys
 195 200 205

Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr
 210 215 220

Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu
 225 230 235 240

Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu

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Ser Gln Leu Gly Glu Asp Tyr Ile Gln Leu His Lys Leu Leu Arg Lys 290 295 300		
Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro 305 310 315 320		
Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly 325 330 335		
Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg 340 345 350		
Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe 355 360 365		
Ile Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro 370 375 380		
Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly 385 390 395 400		
Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp 405 410 415		
Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln 420 425 430		
Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp 435 440 445		
Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly 450 455 460		
Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu 465 470 475 480		
Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu 485 490 495		
Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr 500 505 510		
Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu 515 520 525		
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Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu
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Met Glu Gly Ala Val Gly Gly
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gtg agg agg cgt aac ggg gcg gag gaa agg aga aaa ggg cgc tgg ggc 162
Val Arg Arg Arg Asn Gly Ala Glu Glu Arg Arg Lys Gly Arg Trp Gly
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tcg gcg gga gga agt gct aga gct ctc gac tct ccg ctg cgc ggc agc 210
Ser Ala Gly Gly Ser Ala Arg Ala Leu Asp Ser Pro Leu Arg Gly Ser
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Trp Arg Gly Glu Gln Pro Gly Glu Pro Lys Met Leu Leu Arg Ser Lys
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cct gcg ctg ccg ccg ccg ctg atg ctg ctg ctc ctg ggg ccg ctg ggt 306
Pro Ala Leu Pro Pro Pro Leu Met Leu Leu Leu Leu Gly Pro Leu Gly
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Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro Ala Gln Ala Gln Asp Val
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Val Asp Leu Asp Phe Phe Thr Gln Glu Pro Leu His Leu Val Ser Pro
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Ser Phe Leu Ser Val Thr Ile Asp Ala Asn Leu Ala Thr Asp Pro Arg
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Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu Arg Thr Leu Ala Arg Gly
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Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe Glu Glu Arg Ser Tyr Trp
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Gln Ser Gln Val Asn Gln Asp Ile Cys Lys Tyr Gly Ser Ile Pro Pro

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ctc tat ggt cct gat gtt ggt cag cct cga aga aag acg gct aag atg Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg Arg Lys Thr Ala Lys Met 315 320 325			1074
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Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His
370 375 380

Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu
385 390 395 400

Leu Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys
405 410 415

Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val
420 425 430

Tyr His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn
435 440 445

Leu His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg
450 455 460

Lys Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu
465 470 475 480

Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp
485 490 495

Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser
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Ala Lys Ile Ala Ala Cys Ile
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Gln Gly Ala Pro Ala Gly Thr Ala Pro Thr Asp Asp Val Val Asp Leu
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Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe Leu
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Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu Thr
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Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser Pro
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Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp
85 90 95
ccg gac aag gaa ccg act tcc gaa gaa aga agt tac tgg aaa tct caa 932
Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser Gln
100 105 110
gtc aac cat gat att tgc agg tct gag ccg gtc tct gct gcg gtg ttg 980
Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val Leu
115 120 125
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Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu Arg
130 135 140 145
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Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser
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165 170 175
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Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn Ser
180 185 190
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Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn
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Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys Ala
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His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu Leu
230 235 240

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cca gac agg agc aaa ctc cga gtg tat ctc cac tgc act aac gtc tat Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val Tyr 420 425 430	1892
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cca gtg gat acg tac ctt ctg aag cct tcg ggg ccg gat gga tta ctt Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu Leu 470 475 480	2036
tcc aaa tct gtc caa ctg aac ggt caa att ctg aag atg gtg gat gag Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp Glu 485 490 495	2084
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Lys Ile Ala Ala Cys Ile
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cggttcctca ccttcctgag ctctccacgg ctctgagccc tgtctagagg cttatctcct 240
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c 541